REMARKS

The Office Action of February 25, 2004, has been received and reviewed. Claims 20-46 are hereby canceled without prejudice or disclaimer. New claims 57-121 are hereby added. Claims 20-46 stand rejected under 35 U.S.C. § 112, first paragraph, as assertedly lacking sufficient written description. Claims 20-46 stand rejected under 35 U.S.C. § 103(a) as assertedly being unpatentable over Plasterk *et al.*, in view of Vos *et al.*, Van Leunen *et al.* '94[1], Van Leunen *et al.* '93[2], Hackett *et al.* and Gallegos *et al.*

The present rejections are moot in view of the claim cancellations. The rejections are discussed with respect to the new claims.

Reconsideration is respectfully requested.

Priority Claim:

As suggested in the Office Action, the specification has been amended to recite the priority claim made and perfected in the PCT application.

Rejections under 35 U.S.C. § 112, first paragraph:

Claims 20-46 stand rejected under 35 U.S.C. § 112, first paragraph, as assertedly lacking sufficient written description.

The Office asserts that the claims recite a genus of 3' UTRs, while the specification only discloses the 3' UTR of *glh-2* (page 4 of the Office Action). Therefore, the Office asserts that the claimed genus of UTRs does not have sufficient written description. The Office also asserts that expression in the germline, does not provide a sufficient written description of an identifying feature of the claimed genus of 3' UTRs, "since all of the genes [expressed in the germline] will have that characteristic" (page 4 of the Office Action).

The applicants respectfully point out that, in addition to the 3' UTR of *glh-2*, the specification discloses the use of the 3' UTR of Tc3, *see, e.g.*, page 13, line 14 to page 15, line 17, and the 3' UTR of HIMAR1, *see, e.g.*, page 15, line 19 to page 16, line 25. Therefore, the specification discloses at least three working examples of 3' UTRs that may be used.

"A 'representative number of species' means that the species which are adequately described are representative of the entire genus. .... What constitutes a 'representative number' is an inverse function of the skill and knowledge in the art. Satisfactory disclosure of a 'representative number' depends on whether one of skill in the art would recognize that the applicant was in possession of the necessary common attributes or features of the elements possessed by the members of the genus in view of the species disclosed" (Guidelines for Examination of Patent Applications Under the 35 U.S.C. § 112, ¶1, "Written Description" Requirement, 66 FR 1099, 1106 (2001)).

Since the basic functional characteristics of a 3' UTR are well known in the art, the disclosure of at least three 3' UTRs sufficiently describes the members of the genus. Thus, a person of skill in the art would recognize that the applicants were in possession of the necessary common attributes or features of the genus (*Id.*). Therefore, contrary to the assertion that the specification does not "reasonably convey to one skilled in the art that the Applicant is in possession of the genes that are expressed in the germ line of C. elegans" (page 5 of the Office Action), the specification does reasonably convey to a person of ordinary skill in the art that the applicants were in possession of a genus of 3' UTRs. Moreover, Gallegos *et al.* teaches post-translational regulation by the 3' UTR of *fem-3*, thereby providing a fourth 3' UTR that may be used in the invention, where such post-translational regulation is desired.

Moreover, new claims 70, 72 and 96 specifically recite the 3' UTR of *glh-2*, which the Office acknowledges to have sufficient written description.

For these reasons, it is respectfully submitted that the 35 U.S.C. § 112, first paragraph, rejection does not apply to any of the new claims 57-122.

Rejections under 35 U.S.C. § 103(a):

Claims 20-46 stand rejected under 35 U.S.C. § 103(a) as assertedly being unpatentable over Plasterk *et al.*, in view of Vos *et al.*, Van Leunen *et al.* '94[1], Van Leunen *et al.* '93[2], Hackett *et al.* and Gallegos *et al.* Claims 20-46 have been canceled without prejudice or disclaimer,

thereby rendering the rejection moot. Moreover, new claims 57-122 are not obvious in light of the cited references.

The Office asserts that Plasterk *et al.* discloses methods for integrating desired nucleic acids into other nucleic acid material, including the genome of *C. elegans*. Specifically, the Office asserts that Plasterk *et al.* discloses introduction of the transposase vector in *C. elegans* at columns 3-6 (page 6 of the Office Action). The applicants respectfully disagree with this characterization of Plasterk *et al.*

The primary example of a transposable element used in Plasterk *et al.*, Tc1, was obtained from *C. elegans*. However, Plasterk *et al.* does not disclose transposition **in** *C. elegans*. The most that can be said is that Plasterk *et al.* discloses expression of a Tc1 transposase in somatic cells of *C. elegans* and the use of a nuclear extract, prepared from whole animals producing the Tc1 transposase, to induce a transposition event *in vitro* (*see*, for example, FIG. 3 and col. 6, line 33 to col. 7, line 26 of Plasterk *et al.*). *In vivo* transposition events were conducted in human cells (*see*, for example, col. 10, line 1 to col. 12, line 7 of Plasterk *et al.*), since the primarily purpose of Plasterk *et al.* is directed to gene therapy in humans.

Thus, Plasterk *et al.* does not teach or suggest transposition **in** *C. elegans*, as recited in new claims 57 to 122. Moreover Plasterk *et al.* does not teach or suggest transposition in the germline of *C. elegans*, as recited in claims 59, 72, 73, 81, 85, 86, and 92-122. In addition, Plasterk *et al.* does not teach or suggest the use of an artificial intron in a transposase used in *C. elegans*, as recited in claims 57-76, 83, 107, 111, 113, 117, and 118, nor does Plasterk *et al.* teach or suggest the use of a heterologous transposon in *C. elegans*, as recited in claims 61-67, 74, 77-91, 98-101, 109-112, 116, 117, and 120-122.

The Vos *et al.* reference discloses expression of a Tc1 transposase in the somatic cells of *C. elegans* and the use of an extract prepared from such cells to induce a transposition event *in vitro*, as disclosed in Plasterk *et al.*[1] However, Vos *et al.* does not teach or suggest transposition **in** *C. elegans*, transposition in the germline of *C. elegans*, the use of an artificial intron in the transposase, or the use of a heterologous transposon in *C. elegans*, as recited in claims 57-122.

[1] Note the overlap between the authors of Vos *et al.* and the inventors of Plasterk *et al.*

Van Luenen *et al.* '93[2] discloses somatic expression of the Tc3 transposase under the control of a heat shock promoter and induction of transposition in somatic cells (*see*, van Luenen *et al.* '93 at 2516, first and second column). However, van Luenen *et al.* '93 teaches away from using a heat shock promoter to produce germline transposition, since "the *hsp-16* promoter is only active somatically" (*Id.*)(citations omitted). Hence, van Luenen *et al.* '93 does not teach or suggest transposition in the germline of *C. elegans* (*e.g.*, claims 59, 72, 73, 81, 85, 86, and 92-122), transposition of a heterologous transposon (*e.g.*, claims 61-67, 74, 77-91, 98-101, 109-112, 116, 117, and 120-122), or the use of an artificial intron in the transposase (*e.g.*, claims 57-76, 83, 107, 111, 113, 117, and 118). Therefore, Van Luenen *et al.* '93 does not teach or suggest the claim elements lacking in Plasterk *et al.*, or Vos *et al.*

The applicants agree with the Examiner that these references do not teach or suggest a 3' UTR that is expressed in the germline (page 6 of the Office Action). Moreover, Plasterk *et al.*, Vos *et al.* and Van Luenen *et al.* '93, either alone or in combination, do not teach or suggest an artificial intron, use of a heterologous transposon in *C. elegans*, or germline transposition in *C. elegans*, as recited by claims 57-122.

Gallegos *et al.* is asserted to teach expression of a gene of interest (*lacZ*) in the germline (page 6 of the Office Action). The applicants respectfully disagree. Gallegos *et al.* discloses expression of the gene of interest in somatic cells and teaches away from expression in the germline. For example, "transgenes do not express well in the germ line of *C. elegans* and we did not know *a priori* which somatic tissues might contain *fem-3* repressor activity, each *lacZ::fem-3* construct was fused to the *C. elegans hsp16* heat shock promoter. This promoter drives expression in various somatic tissues following heat shock (Gallegos *et al.* at the paragraph spanning pages 6338-6339) (emphasis added) (citations omitted). Thus, while Gallegos *et al.* studied the post-transcriptional regulatory effects of the *fem-3* UTR, which produces its phenotype in the germline of *C. elegans*, the authors do not teach or suggest expression in the germline. Specifically, Gallegos *et al.* teaches away from expression in the germline, particularly, with the heat shock promoter. Because Gallegos *et al.* teach away from expression in the germline, it is improper to combine the references (*see*, MPEP §

2145(X)(D)(2)). In addition, Gallegos *et al.* does not teach or suggest an artificial intron, use of a heterologous transposon in *C. elegans*, or germline transposition in *C. elegans*, as recited by claims 57-122.

Finally, Hackett *et al.* is generally directed to transposition in vertebrates using the transposase and transposon isolated from a teleost fish (Hackett *et al.*, col. 3, lines 18-58), and does not teach or suggest transposition in *C. elegans*, as recited in claims 57-122. Moreover, Hackett *et al.* does not teach or suggest transposition in the germline of *C. elegan* (*e.g.*, claims 59, 72, 73, 81, 85, 86, and 92-122), insertion of an artificial intron into a transposase gene (*e.g.*, claims 57-76, 83, 107, 111, 113, 117, and 118), or transposition of a heterologous transposon in *C. elegans*, or transposition of a heterologous transposon in *C. elegans* (*e.g.*, claims 61-67, 74, 77-91, 98-101, 109-112, 116, 117, and 120-122).

Since none of the cited references teach or suggest all of the claim elements, including transposition in the germline of *C. elegans*, expression of a transposase gene having an artificial intron, and/or transposition of a heterologous transposon in *C. elegans*, the references, either alone or in combination, cannot anticipate or make obvious the claimed invention. Furthermore, Gallegos *et al.* teaches away from germline expression and Van Luenen *et al.* '93 teaches away from the use of the heat shock promoter for germline expression. Therefore, there is no motivation to combine the references.

Moreover, there has been a long-felt need for a mutational system in *C. elegans* that would allow quick identification of the mutated gene (*see, e.g.*, the abstract of Bessereau *et al.* (2001) Mobilization of a *Drosophila* transposon in the *Caenorhabditis elegans* germ line, *Nature* 413:70-74; and http://elegans.imbb.forth.gr/nemagenetag/home.html). Despite this need, no such system was described until the present invention. The long-felt need for a mutagenesis system that allows for the rapid identification of the mutated gene, especially when combined with the teaching away provided in Van Luenen *et al.* '93 and Gallegos *et al.*, demonstrates the non-obvious nature of the claimed invention.

Accordingly, reconsideration and withdrawal of the rejection is respectfully requested.

CONCLUSION

In the event questions remain after consideration of these remarks and amendments, the Office is kindly requested to contact applicants' representative at the number given below.

Respectfully submitted,

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